FLGDK32.001APC

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant	:	Rauch et al.
App. No	:	10/590,686
Filed	:	June 15, 2007
For	:	AQUEOUS SOLUTION FOR USE AS MEDIUM FOR THE SPECIFIC BINDING REACTION OF A BINDING PAIR
Examiner	:	Haq, Shafiqul
Art Unit	:	1641
Conf No.	:	2841

DECLARATION UNDER 37 C.F.R §1.132

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

1. I, Petra Rauch, am an inventor of the present application.

2. I have extensive experience in the field of immunology for many years. My Curriculum Vitae is attached herewith as Exhibit A.

3. The human anti-mouse antibody (HAMA) effect is depicted schematically in Figure 1. In the absence of the HAMA effect, analyte is sandwiched between immobilized capture antibody and labeled detecting antibody (panel A). As illustrated, HAMA can cross-link capture antibody and labeled detecting antibody, resulting in a false positive signal (panel B). Alternatively, HAMA may bind to capture antibody or detecting antibody resulting in a false negative signal (panels C and D).

4. I examined the reduction of HAMA-effects by Sample Buffer as disclosed in the presently claimed methods. HAMA-positive human serum samples were pre-diluted 1:10 with Sample Buffer or with the commercially provided dilution buffer (MEDAC VIR-DIL). HAMA-effects were measured by using a CE-marked "HAMA-ELISA-KIT" (Medac, Germany). HAMA concentrations of greater than 40 ng/ml are defined as positive (according the kit manufacturer). Referring to Figure 2, Sample Buffer according to the presently claimed methods reduced all HAMA-effects of the tested HAMA-positive samples.

5. I examined the anti-HAMA effect with regard to HAMA-positive sera samples Nos. 14 und 24. Referring to Figure 3, Sample Buffer-TRIS (SB-TRIS) and Sample Buffer-MES (SB-MES) have the same effect. With respect to serum 14, the anti-HAMA effect of Sample Buffer-PBS (SB-PBS) is weaker compared to the buffers SB-TRIS and SB-MES.

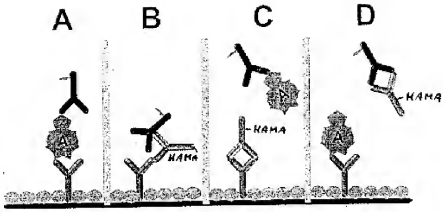
6. I examined the anti-HAMA effect of Sample Buffer-PBS (3rd column) and Sample Buffer-TRIS (2nd column) on HAMA-positive serum 120566-24. Referring to Figure 4, the HAMA-effect is strongly reduced using the sample buffer according to the invention (2nd and 3rd column) compared to the standard buffer (1st column). However, using the sample buffer containing PBS does not reduce the disturbing HAMA effect quite as strong as using the sample buffer containing TRIS.

7. Although the foregoing experiments were conducted with HAMA-positive human samples, one skilled in the art can readily conclude that the same reduction of undesired effects can be achieved in samples containing other heterophilic antibodies. Based on the discussion in paragraph 3 of this declaration, one skilled in the art would have no difficulty understanding that the same effects can be avoided in the presence of antibodies directed to other species.

8. I declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful, false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or patent issuing therefrom

Dated: 30/Nov/2009 By: _____

Figure 1. Schematic Representation of HAMA Effects



A: Normal assay, without human anti-mouse antibody (HAMA) effects. The analyte (A) is sandwiched between immobilized capture antibody (gray) and labeled detecting antibody (black).

B: HAMA cross-links capture antibody and labeled detecting antibody resulting in a false positive signal.

C: HAMA binds to capture antibody resulting in a false negative signal.

D: HAMA binds to labeled detecting antibody resulting in a false negative signal.

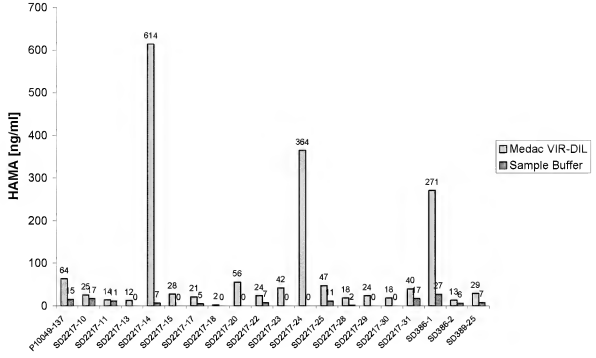

HAMA [ng/ml]
700
600
500
400
300
200
100
0
Medac VIR-DIL
Sample Buffer
64
5
25
7
14
1
12
0
614
7
28
0
21
2
2
0
56
0
24
7
42
0
364
0
47
1
18
2
24
0
18
0
40
7
271
37
13
6
29
7
P10049-137
SD2217-10
SD2217-11
SD2217-13
SD2217-14
SD2217-15
SD2217-17
SD2217-18
SD2217-20
SD2217-22
SD2217-23
SD2217-24
SD2217-25
SD2217-28
SD2217-29
SD2217-30
SD2217-31
SD386-1
SD386-2
SD389-25

Fig. 2

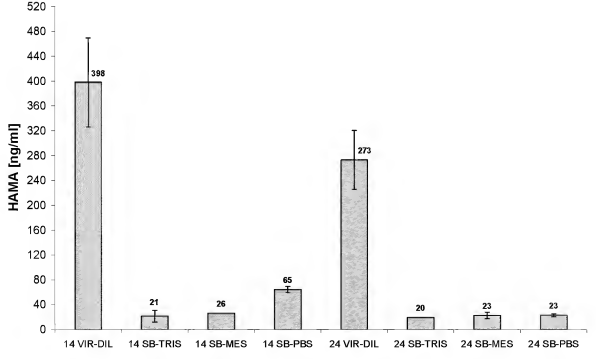

HAMA [ng/ml]
520
480
440
400
360
320
280
240
200
160
120
80
40
0
398
21
26
65
273
20
23
23
14 VIR-DIL
14 SB-TRIS
14 SB-MES
14 SB-PBS
24 VIR-DIL
24 SB-TRIS
24 SB-MES
24 SB-PBS

Fig. 3

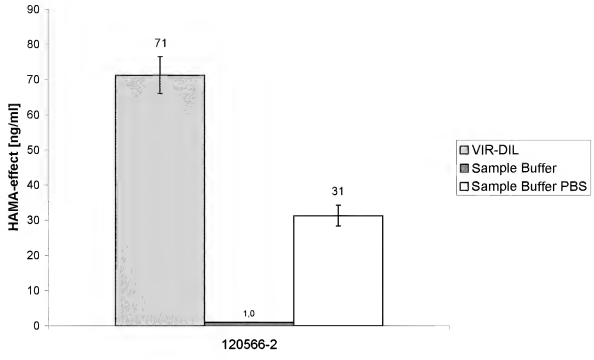

90
80
70
60
50
40
30
20
10
0
HAMA-effect [ng/ml]
71
1,0
31
120566-2
VIR-DIL
Sample Buffer
Sample Buffer PBS

Fig. 4

EXHIBIT A

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Curriculum Vitae

Personal details

Date of Birth	4th of February, 1967
Place of Birth	Paderborn, Germany
Marital status	married, two children

Education

1987 - 1995	Studies of chemistry and biology, University of Cologne and Heinrich-Heine-University Düsseldorf
1995	Master' s degree in Biology (Diplom), Düsseldorf
1995 - 1998	Doctoral Thesis

Professional Experience

1998 - 2002	Senior Scientist at Institut für Chemo- und Biosensorik e.V. (Münster, Germany
2002 - 2003	Group manager „Preanalytics and Assaydevelopment", ICB GmbH (Münster, Germany)
Since 2004	Cofounder of CANDOR Bioscience GmbH, Managing director and Head of Research and Development

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Weißensberg, 30/04/2007